AUTOMATIC TIME SEQUENCE ALIGNMENT IN CONTRAST ENHANCED MRI BY MAXIMIZATION OF MUTUAL INFORMATION

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Abstract- **The use of contrast medium allows joining the high-resolution anatomical information provided by standard magnetic resonance with functional information obtained by means of the diffusion of contrast agent in tissues or in the vascular net. To effectively use this kind of images for medical diagnosis, quantitative analysis should be performed. We propose an automatic registration procedure based on maximization of the mutual information that address the requirement of fast and automatic tools for quantitative analysis of contrast medium enhanced MR images. Two optimization algorithms for maximization of the mutual information are discussed, taking into account both time performance and registration quality. We present also preliminary results on cardiac and wrist MR images showing that misalignments and artifacts introduced by patient movement during the examination are greatly reduced by our application.**

Keywords - Magnetic Resonance, Image Registration, Mutual Information, Contrast Enhanced MRI

I. INTRODUCTION

The use of contrast medium (CM) to enhance the information provided by Magnetic Resonance is a growing technique. In fact, the use of contrast enhanced images allows to join the high-resolution anatomical information provided by standard MR with functional information obtained by means of the diffusion of contrast medium in tissues or in vascular net. The way in which the contrast medium evolve during time can provide information about the tissue functionality and perfusion.

In order to follow the diffusion of contrast medium, several images of the same anatomical district are acquired during time, starting from the injection of contrast medium. The so called time/intensity (T/I) curve can be evaluated measuring the intensity value of each image pixel during time. An example of the use of perfusion analysis in MRI is myocardial perfusion imaging with Gadolinium-DTPA as contrast agent, that allows to assess the extent and type of tissue injury after myocardial infarction. Contrast enhanced MR images can be also useful in medical examination of other districts, such as extremities (knees, ankles, wrists and elbows) and brain.

Quantitative evaluation of the contrast agent distibution during time implies to find the corresponding pixels in all temporal frames. Usually, the acquisition protocol is made to obtain spatial alignment of all frames. Therefore, each pixel in a image frame should correspond to the pixels in the other frames with the same geometrical coordinates. So that, the segmentation of the district of interest can be done on the best image, i.e. the one with the best contrast to noise ratio. This surely enhances both the reliability and the performance of the analysis.

Unfortunate, obtaining spatially aligned images is a difficult task, mainly due to the movement of the anatomical district under examination. Therefore, a misalignment correction, also named image registration, is needed in post-processing phase. A lot of methods were proposed to address the general medical image registration problem [1,2]. About the present problem, Yang *et alt*. proposed to extract some geometrical features from each frame and to perform the image registration by registering the extracted geometrical features [3]. Because a single multiphase 3D study can consist of hundreds of images, manual or semi-automatic segmentation of a so large data set is a time-consuming task and is affected by intra-observer and inter-observer variability. So that, automatic tools should be used. On the other hand, most of the automatic image segmentation algorithms are very sensitive to noise. Although the acquisition parameters can be optimized regarding SNR and contrast, such methods usually result in a significant increase in the overall acquisition time. This is absolutely unreliable when we need high temporal resolution. Moreover, many automatic segmentation algorithm are model-based and can be used only to segment a specific anatomical district .

We prefer to apply voxel-based methods that operate directly on the image gray values, and are effective in our problem due to the high degree of similarity between involved images. Moreover, this kind of algorithm can be applied without modifications to images representing every organs. Along voxel-based methods we select mutual information as registration parameter, because this was demonstrated effective in a large set of applications.

The goal of this study is to apply a new automatic analysis procedure starting from contrast enhanced MR images in order to correct the images misalignment in post-processing phase. The method has been tested on clinical MR images data of the heart and the wrist.

II. METHODOLOGY

A. Mutual Information

The Mutual Information (MI) concept comes from information theory, measuring the dependence between two variables or, in other words, the amount of information that one variable contains about the other [4]. The mutual information MI between two data set X and Y can be defined as:

$$MI(X;Y) = H(X) + H(Y) - H(X,Y)$$

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where H(.) is the entropy of a random variable, and is defined as:

$$H(X) = -\sum_{x_i \in \Omega_X} \log[P(X = x_i)] \cdot P(X = x_i)$$

The join entropy of two random variables X and Y is:

$$H(X,Y) = -\sum_{x_i \in \Omega_X} \sum_{y_j \in \Omega_Y} \log[P(X = x_i, Y = y_j)] \cdot P(X = x_i, Y = y_j)$$

Entropy can be interpreted as a measure of the information associated with the variable. The mutual information measures the relationship between two random variables: if the two variables are independent, $H(X,Y) = H(X) + H(Y)$ and MI=0. If one variable provides some information about the second one, the MI becomes greater then zero.

B. Registration Algorithm

The MI registration criterion states that the MI of the image intensity values of corresponding voxel pair is maximal if the images are geometrically aligned. Because no assumption is made about the nature of the relation between the image intensities, this criterion is very general and powerful [5, 6]; so that, it can be applied automatically at any image in the sequence also during contrast medium transit.

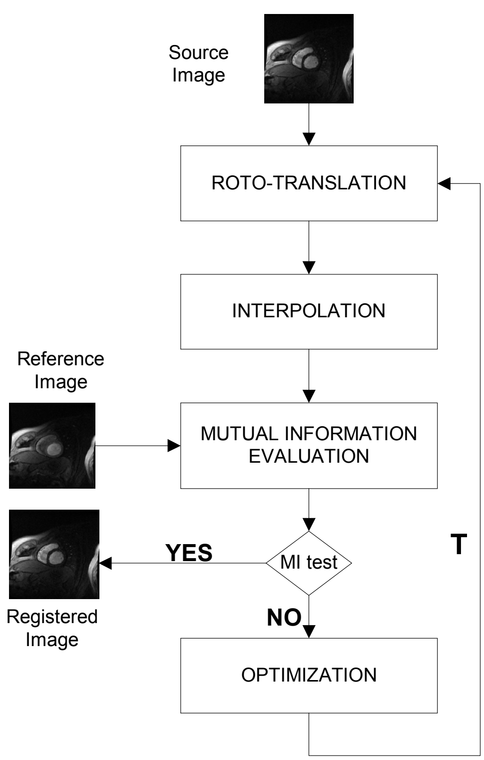

Fig. 1: Flow chart of the registration algorithm

Say u(X) as the reference image data set; X represents the pixels (or voxels) coordinates and u(X) the intensity value. Say v(X) as the image data set that have to be registered with the reference data set u(X). The better rigid transformation T can be found maximizing the mutual information between u(X) and v(T(X)).

$$MI[u(X), v(T\ (X))] =$$
$$= H(u(X)) + H(v(T(X))) - H(u(X), v(T(X)))$$

Finding the T matrix that maximize the value of MI implies the solution of an optimization problem with three (in case of 2D images) or six (in case of 3D images) variables.

In our problem, we have to find the best alignment not only between two images, but along all frames in the temporal sequence. In order to reduce the algorithm complexity and the related processing time, we choose to reduce the problem to a sequence of MI maximization between image pairs. The way in which we choose the pairs will be shown in the following, now we can illustrate the registration algorithm between two images, as showed in Fig 1. First, the MI between the reference image and the image under examination is evaluated. An optimization algorithm is used in order to estimate the best roto-translation matrix T; the matrix is used to rotate and translate the image. An interpolation operation is also required. If the result is satisfactory, the procedure ends; if not, a new roto-translation matrix is evaluated and a new loop is executed. The whole process is automatically executed.

About image interpolation, a lot of work was done in order to find the best interpolation method [7]: we use two solutions: a simple linear interpolation method during the MI maximum research to obtain the best time performance and an interpolation algorithm optimized for MR images [8] in the last step to compute the final image.

C. Optimization methods

The problem of finding the parameters set that maximize a multi-variable function is called optimization problem. The optimization algorithm should find the rotation and translation parameters that will maximize the MI. The main troubles are the presence of MI local maxima and the long processing time required by a lot of optimization algorithms.

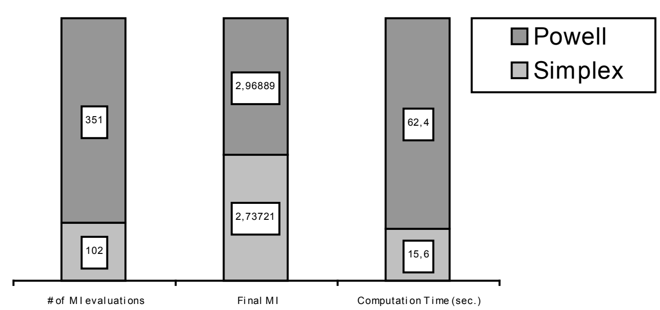

Fig. 2. Performance of simplex and Powell optimization methods

We have tested two optimization algorithms, the simplex algorithm and the Powell algorithm. The main advantage of the downhill simplex method [9] is about time performance, because the simplex method requires only function evaluations - not derivatives – and so may be more reliable than other optimization methods. The Powell method [10] is more effective respect to the simplex method, especially for avoiding local maxima. On the other hand, it requires a long computation time. Fig. 2 shows the results of the two optimization methods applied to two test images. The Powell method leads to best results (i.e. greater MI), the simplex method is less computationally expensive.

In order to obtain a effective image registration, an important aspect is the way to choose the pair of images to be registered. The first idea is to register each image with the previous one. Because the CM diffuses in continuous manner, two consecutive images are almost similar in the sequence, so the registration algorithm can better correct the misalignment. On the other hand, an error in the registration of one image pair will affect the alignment of the whole temporal sequence. A second approach is to register all frames respect to one image in the sequence. This one is selected by the user as the image that has to be used to perform the segmentation, i.e. the image in which the district of interest is best delineated. We have used the following approach: first, all frames are registered using the simplex algorithm respect to the image in the sequence selected by the user. After, a more accurate registration using the Powell method is performed registering each image with the previous one. The search range for the T matrix elements is reduced in this second step to reduce the prcessing time. This approach leads in many cases to the best results.

III. Results

The method has been tested on two image data sets. The first one is a set of Gd-DTPA contrast enhanced cine cardiac MRI acquired using a GE Signa Horizon LX System 1.5T. A cardiac array coil has been used, with cardiac-gated fast gradient echo – echo train (FGRET) sequence.

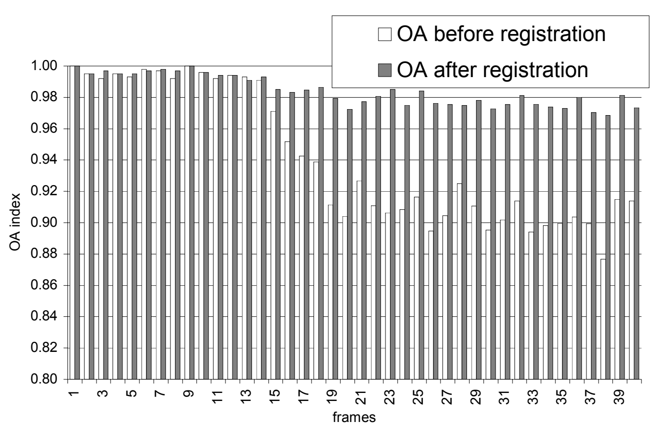

Fig. 3: OA index before and after registration for cardiac images

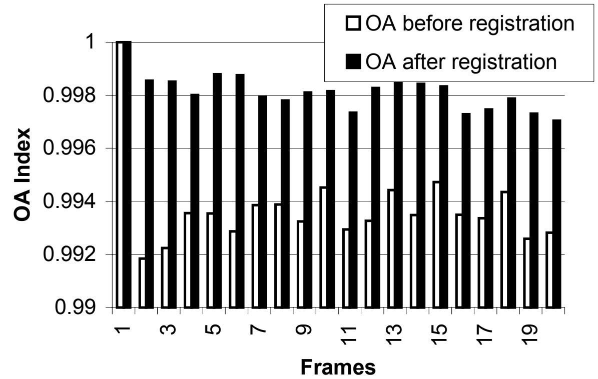

Fig. 4: OA index before and after registration for wrist images

A total of 320 images were acquired, consisting on 8 short axis slices, each one with 40 temporal frames. For each temporal image and for each spatial slice, the endocardial contour has been manually traced before and after the registration procedure; we used the overlapping area index (OA) as an index of image registration degree. Overlapping area is the common area between the region selected in the developing image and the reference one, normalized by the reference area.

In order to quantitatively evaluate the effectiveness of the MI-based registration technique, images corresponding to a normal volunteer were firstly analyzed: because such images have been acquired during breath-hold, we can consider them as already spatially aligned. For normal aligned images, the mean OA value was equal to 0.98, with SD = 0.094. The same OA index evaluation procedure has been performed on the patients images, before and after registration procedure. Fig. 3 shows the value of OA index for each frame before and after registration.

The second data set is a set of wrist images acquired by an ESAOTE Artoscan MR acquisition device. ESAOTE Artoscan is an office-size scanner which provides high-quality images of the extremities only (knees, ankles, wrists and elbows). It includes a permanent magnet with an 0.18 T field.

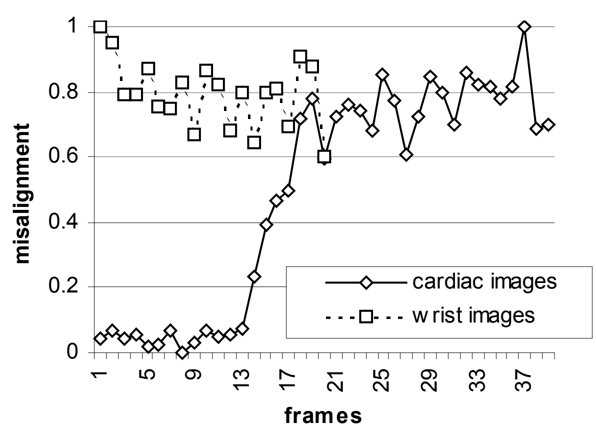

Fig. 5: Frames misalignment (normalized) for cardiac and wrist images

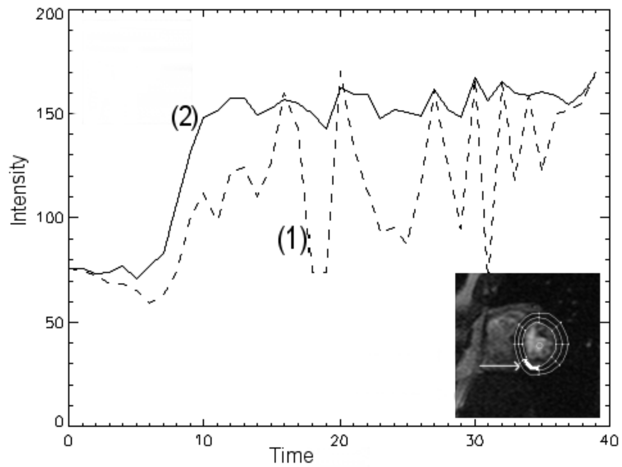

Fig. 6: Time/Intensity curves before (1) and after (2) registration for myocardial perfusion images.

The SE (T1=16ms, T2=100ms) sequence was used to acquire 3 sections of the wrist during the diffusion of a CM. A total of 21 frames was acquired for each slice. The OA index was evaluated as in the previous data set, manually tracing the anatomical district under examination before and after application of the registration procedure. Fig. 4 shows the OA index before and after registration for wrist images.

It is interesting to note that in order to improve the registration algorithm, some a-priori information about the misalignment can be included in the procedure. As it is shown in Fig. 5, the misalignment value in wrist images is randomly distributed respect to the acquisition time. Instead, in cardiac perfusion images, until the patient is able to hold his breath, the misalignment value is small. After that, the misalignment increases. The misalignment is measured respect to the image 1 for the wrist and the image 8 for the myocardium. This kind of a-priori information can be used to limit the research range of the optimization algorithm, improving both the speed and the effectiveness of the registration procedure.

Fig. 6 shows an example of a time/intensity curve extracted from a myocardium region before and after application of the registration algorithm. The artifacts present in the T/I curve before registration are greatly reduced with the application of the MI based registration algorithm.

IV. DISCUSSION AND CONCLUSIONS

The use of an automatic registration procedure based on maximization of the mutual information seems to be effective in order to address the requirement of fast and automatic tools for quantitative analysis of CM enhanced MR images.

The quantitative index OA (Overlapping Area) was introduced in order to measure in quantitative way the algorithm effectiveness. Preliminary results on cardiac and wrist images show that misalignments and artefacts introduced by patient movement during the examination are greatly reduced.

Different approaches about the choice of the optimization algorithm for maximization of the mutual information between to images are discussed, taking in account both time performance and registration quality. Some preliminary results are also presented about the use of a-priori information to improve the registration procedure.

Contemporary registration of several temporal frames is still an open problem. In this work, our approach was to reduce the problem to a lot of registration operations between image pairs. The development of a global registration algorithm should improve the registration quality. Perhaps, the development of a dedicated optimization methods based on new techniques such as evolutionary computing and the use of parallel computing will needed in order to obtain an effective global registration algorithm.

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REFERENCES

[1] P. A Van Den Elsen, E. J. D. Pol, M. A. Viergever, “Medical Image Matching – A Review with Classification,” *IEEE Engineering in medicine and biology* 12(1), 1993, pp. 26–39.

[2] J. B. A. Maintz, M. A. Viergever, “A survey of medical image registration,“ *Medical Image Analysis*, 2(1), 1998, pp. 1-36.

[3] X. Yang, Y. Taeymans, P. Carlier, P. Verstraeten, K. Brunfaut, M. Cornelis, “Computer Aided Measurement of Local Myocardial Perfusion in MRI,” *IEEE Computers in Cardiology 1993*, Proceedings, 1993 pp 365 –368.

[4] A. Papoulis, *Probability, Random Variables and Stochastic Processes*, McGraw-Hill, Inc., third edition, 1991.

[5] P. Viola, W.M. Wells, “Alignment by Maximization of Mutual Information,” *Int. Jour. of Comp. Vision*, 24(2), 1997, pp. 137-154.

[6] F. Maes, A. Collignon, D. Vandermeulen, G. Marchal, P. Suetens, “Multimodality image registration by maximization of mutual information,” *IEEE Transactions on Medical Imaging*, vol. 16, no. 2, April 1997, pp. 187-198.

[7] G. J. Grevera, J. K. Udupa. “An Objective Comparison of 3D Image Interpolation Methods,” *IEEE Transactions on Medical Imaging*, vol. 17, no. 4, August 1998, pp. 642-652.

[8] J.V. Hajnal, N. Saeed, E.J. Soar, A. Oatridge, I.R. Young, G.M. Bydder. ”A Registration and Interpolation Procedure for Subvoxel Matching of Serially Acquired MR Images,” *Journal of Comp. Ass. Tomography*, vol. 19(2), March/April 1995, pp. 289-296.

[9] J. A. Nelder and R. Mead. A simplex method for function minimization. *Computer Journal*, 7:308-313, 1965.

[10] W. H. Press, S.A. Teukolsky, W.T. Vetterling, B. P. Flannery, *Numerical Recipes in C. 2nd ed.*, Cambridge University Press, 1992.